REMARKS

Claims 24-57 are pending. Claims 50-57 are allowed. Claims 24, 25, and 45 are rejected. Claims 26-44 and 46-49 are objected to. Claims 32-42, 46-49 and 51-57 have been amended to provide proper antecedent basis. Claims 58-67 are newly added. The new claims 58-65 serve to make the elements of the Markush groups separate dependent claims. Support is found in the claims. No new matter was added. Support for new claims 66 and 67 is found in the claims. The pending claims are attached for the Examiner's convenience as Appendix A. A copy of claims showing changes made is attached as Appendix B.

Response to Rejection Under 35 U.S.C. § 102(e)

Claims 24, 25, and 45 are rejected under 35 U.S.C. § 102(e) as beinganticipated by Read *et al.* U.S. Patent No. 6,420,169 (hereinafter "Read"). Applicants respectfully traverse.

The Read invention is drawn to a method and apparatus for forming polynucleotides or polypeptides on a surface. Figure 25, which was noted by the Examiner, in particular, is a schematic illustration of a "pure" binary masking strategy. In that particular embodiment, a mask (m1) allows illumination of half of the substrate. The substrate is then exposed to building block A, which binds at the illuminated regions. Next, another mask (m2) allows illumination of half of the previously illuminated region, while it does not illuminate half of the previously illuminated region. The building block B is then added which binds to the illuminated regions from m2.

In contrast, claim 24 teaches a composition comprising a substrate with a surface with discrete sites (wells) at a density of at least 100 discrete sites per 1 mm^2 and a population of microspheres randomly distributed in the wells. The population of beads comprises at least a first and a second subpopulation. The beads also comprise a bioactive agent. Finally, the sites can contain only a single microsphere. Claim 25 teaches a composition similar to claim 24 wherein there is a population of microspheres, and each microsphere comprises a bioactive agent and the microspheres are distributed on a patterned surface. Finally, claim 45 teaches a method of determining the presence of at least a first and second target analyte in a sample. The method includes contacting the sample with a composition that includes a substrate with a patterned surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation. The first subpopulation comprises a first bioactive agent and the second subpopulation comprises a second bioactive agent. The microspheres are randomly distributed on the surface such that

the discrete sites contain only one microsphere. Finally, the presence of the first and second target analyte is determined.

The law is well established that in order to anticipate a claim, the prior art must disclose "each and every element" of the claimed invention. SSIH Equipment S.A.v. U.S. Inc. Int'l. Trade Commission, 218 USPQ 678, 688 (Fed. Cir. 1983). As stated by the Federal Circuit in In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990), "[f]or a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference." (Emphasis added). See also Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc., 33 USPQ2d 1496 (Fed. Cir. 1995).

With regard to claim 24, each and every element is not present in Read, since nowhere in the Read patent is a density of 100 discrete sites, or 100 wells per 1 mm^2 mentioned. Moreover, the Read patent does not teach a first and second subpopulation of microspheres randomly distributed in wells. Read also does not teach a single microsphere per well.

Similarly, each and every element of claim 25 is not present in Read, because microspheres randomly distributed on sites, wherein said sites are at a density of 100 discrete sites, or 100 wells per 1 mm^2 is not taught. Also, Read fails to disclose such distribution wherein there is a single microsphere per well.

Finally, with regard to claim 45, each and every element is not present in Read, for similar reasons as described above. That is, Read does not teach a random distribution of microspheres on the surface of a substrate such that discrete sites on the substrate only contain one microsphere. Hence, Read does not teach each element of the present invention.

Accordingly, Applicant submits that Read fails to teach each and every element of claims 24, 25, and 45. Accordingly, Applicant respectfully requests the Examiner to withdraw this rejection.

CONCLUSION

In light of the amendments, Applicant submits that all currently pending claims now in condition for allowance. An early notification of such is solicited. Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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Appendix A
Pending Claims

24. A composition comprising:

a) a substrate with a surface comprising discrete sites at a density of at least 100 discrete sites per 1 mm^2, said discrete sites comprising wells; and

b) a population of microspheres randomly distributed in said wells, said population comprising at least a first and a second subpopulation, said microspheres comprising a bioactive agent, and wherein said sites can have only a single microsphere.

25. A composition comprising:

a) a substrate with a patterned surface comprising discrete sites, said substrate comprising discrete sites at a density of at least 100 discrete sites per 1 mm^2; and

b) a population of microspheres, randomly distributed on said sites, wherein each microsphere comprises a bioactive agent; and
wherein said sites can have only a single microsphere.

26. A composition according to claim 24 or 25 wherein said substrate is a fiber optic bundle.

27. A composition according to claim 24 or 25 wherein said substrate is selected from the group consisting of glass and plastic.

28. A composition according to claim 24 wherein said population of microspheres comprises at least a first and a second subpopulation, wherein the microspheres of said first subpopulation of microspheres are a different size than the microspheres of said second subpopulation.

29. A composition according to claim 24 or 25 wherein said bioactive agent comprises a protein.

30. A composition according to claim 29 wherein said protein is selected from the group consisting of enzymes and antibodies.

31. A composition according to claim 24 or 25 wherein said bioactive agent is a nucleic acid.

32. (Amended) A composition according to claim 66 wherein said population of microspheres comprises at least a first and a second subpopulation, wherein the microspheres of said first subpopulation of microspheres are a different size than the microspheres of said second subpopulation.

33. (Amended) A composition according to claim 24, 66, 28, or 32 wherein said first and said second subpopulations comprise a first and a second bioactive agent, respectively.

34. (Amended) The composition according to claim 33, wherein said first and second subpopulations further comprise a first and a second optical signature, respectively.

35. (Amended) A composition according to claim 34 wherein said at least one of said optical signatures comprises at least one chromophore.

36. (Amended) A composition according to claim 34 wherein said at least one of said optical signatures comprises at least one fluorescent dye.

37. (Amended) A composition according to claim 36 wherein said fluorescent dye is entrapped within said microspheres.

38. (Amended) A composition according to claim 36 wherein said fluorescent dye is attached to said microspheres.

39. (Amended) A composition according to claim 34 wherein said optical signature comprises at least two fluorescent dyes.

40. (Amended) A composition according to claim 66 wherein said bioactive agent comprises a protein.

41. (Amended) A composition according to claim 40 wherein said protein is selected from the group consisting of enzymes and antibodies.

42. (Amended) A composition according to claim 66 wherein said bioactive agent is a nucleic acid.

43. A composition according to claim 24 or 25 wherein said bead is covalently associated with the well.

44. A composition according to claim 24 or 25 wherein said bead is non-covalently associated with the well.

45. A method of determining the presence of at least a first and second target analyte in a sample comprising:

a) contacting said sample with a composition comprising:

i) a substrate with a patterned surface comprising discrete sites; and

ii) a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and said

second subpopulation comprises a second bioactive agent, wherein said microspheres are randomly distributed on said surface such that said discrete sites contain only one microsphere; and

b) determining the presence of said first and second target analyte.

46. (Amended) A method according to claim 45 wherein said substrate is a optical fiber bundle and said microspheres are located within wells at a first terminal end of said bundle.

47. (Amended) A method according to claim 45 further comprising identifying the location of said first and second bioactive agent on said substrate.

48. (Amended) The method according to claim 45, wherein said discrete sites are wells.

49. (Amended) The method according to claim 45, wherein said substrate is selected from the group consisting of glass and plastic.

50. A method of making a composition comprising:

a) providing a patterned surface comprising individual sites on a substrate;

b) randomly distributing microspheres on said surface such that said individual sites contain microspheres, wherein said sites can have only a single microsphere, and wherein said microspheres comprise at least a first and a second subpopulation comprising:

i) a first and second bioactive agent, respectively; and

ii) a first and second optical signature, respectively;

c) detecting said first and second optical signatures while said microspheres are distributed on said surface; and

d) correlating the location of at least one individual site on the array with the bioactive agent at that particular site.

51. (Amended) A method according to claim 50, wherein said distributing comprises serially adding said subpopulations to said sites.

52. (Amended) A method according to claim 50, wherein said substrate is a fiber optic bundle.

53. (Amended) A method according to claim 50, wherein said substrate is selected from the group consisting of glass and plastic.

54. (Amended) A method according to claim 50, wherein said sites are wells.

55. (Amended) A method according to claim 45 or 50, wherein said bead is covalently attached to the well.

56. (Amended) A method according to claim 45 or 50, wherein said bead is non-covalently attached to the well.

57. (Amended) A method according to claim 45 or 50, wherein said bioactive agent is a nucleic acid.

58. (New) A composition according to claim 27 wherein said substrate is glass.

59. (New) A composition according to claim 27 wherein said substrate is plastic.

60. (New) A composition according to claim 30 wherein said protein is an enzyme.

61. (New) A composition according to claim 30 wherein said protein is an antibody.

62. (New) A composition according to claim 41 wherein said protein is an enzyme.

63. (New) A composition according to claim 41 wherein said protein is an antibody.

64. (New) A method according to claim 49 or 53 wherein said substrate is glass.

65. (New) A method according to claim 49 or 53 wherein said substrate is plastic.

66. (New) A method according to claim 25, wherein said population of microspheres comprises at least a first and a second subpopulation.

67. (New) A method according to claim 45 or 50 when said bioactive agent is a protein.

Appendix B
Marked Up Version of the Claims

32. (Amended) A composition according to claim [25] 66 wherein said population of microspheres comprises at least a first and a second subpopulation, wherein the microspheres of said first subpopulation of microspheres are a different size than the microspheres of said second subpopulation.

33. (Amended) A composition according to claim 24, 66, [or] 28, or 32 wherein said first and said second subpopulations comprise a first and a second bioactive agent, respectively.

34. (Amended) The composition according to claim [32] 33, wherein said first and second subpopulations further comprise a first and a second optical signature, respectively.

35. (Amended) A composition according to claim [33] 34 wherein said at least one of said optical signatures comprises at least one chromophore.

36. (Amended) A composition according to claim [33] 34 wherein said at least one of said optical signatures comprises at least one fluorescent dye.

37. (Amended) A composition according to claim [35] 36 wherein said fluorescent dye is entrapped within said microspheres.

38. (Amended) A composition according to claim [35] 36 wherein said fluorescent dye is attached to said microspheres.

39. (Amended) A composition according to claim [33] 34 wherein said optical signature comprises at least two fluorescent dyes.

40. (Amended) A composition according to claim [32] 66 wherein said bioactive agent comprises a protein.

41. (Amended) A composition according to claim [32] 40 wherein said protein is selected from the group consisting of enzymes and antibodies.

42. A composition according to claim [32] 66 wherein said bioactive agent is a nucleic acid.

46. (Amended) A method according to claim [39] 45 wherein said substrate is a optical fiber bundle and said microspheres are located within wells at a first terminal end of said bundle.

47. (Amended) A method according to claim [39] 45 further comprising identifying the location of said first and second bioactive agent on said substrate.

48. (Amended) The method according to claim [39] 45, wherein said discrete sites are wells.

49. (Amended) The method according to claim [39] 45, wherein said substrate is selected from the group consisting of glass and plastic.

51. (Amended) A method according to claim [44] 50, wherein said distributing comprises serially adding said subpopulations to said sites.

52. (Amended) A method according to claim [44] 50, wherein said substrate is a fiber optic bundle.

53. (Amended) A method according to claim [44] 50, wherein said substrate is selected from the group consisting of glass and plastic.

54. (Amended) A method according to claim [44] 50, wherein said sites are wells.

55. (Amended) A method according to claim [39 or 44] 45 or 50, wherein said bead is covalently attached to the well.

56. (Amended) A method according to claim [39 or 44] 45 or 50, wherein said bead is non-covalently attached to the well.

57. (Amended) A method according to claim [39 or 44] 45 or 50, wherein said bioactive agent is a nucleic acid.

The following claims are new:

--58. (New) A composition according to claim 27 wherein said substrate is glass.

59. (New) A composition according to claim 27 wherein said substrate is plastic.

60. (New) A composition according to claim 30 wherein said protein is an enzyme.

61. (New) A composition according to claim 30 wherein said protein is an antibody.

62. (New) A composition according to claim 41 wherein said protein is an enzyme.

63. (New) A composition according to claim 41 wherein said protein is an antibody.

64. (New) A method according to claim 49 or 53 wherein said substrate is glass.

65. (New) A method according to claim 49 or 53 wherein said substrate is plastic.

66. (New) A method according to claim 25, wherein said population of microspheres comprises at least a first and a second subpopulation.

67. (New) A method according to claim 45 or 50 when said bioactive agent is a protein.--